REMARKS

Status of the Claims

Claims 6-17 are pending in this application. Claims 1-5 have been canceled. Claims 9-17 have been added. Claims 6 and 8 have been amended to change dependency from canceled claim 1. Applicants submit that no new matter has been added by the above claim amendments.

Objection to the Specification

The Examiner objects to the specification for a typographical error describing the vector. Applicants amend the specification at page 7 to correct "pAxcwt" to "pAxCAwt". This error is clearly a typographical error. No new matter has been added. Please see page 13, line 25. As such, the objection should be withdrawn.

Objection to the Claims

The Examiner objects to claim 6 for a typographical error. Applicants amend claim 6 to correctly spell transgenic. As such, the objection should be withdrawn.

Rejections under 35 USC 112, first paragraph

The Examiner rejects claims 1-8 as not enabled by the specification. Allegedly the specification does not teach how GFP,

to make the colored pearl, is secreted from the mantle during pearl formation. The Examiner also states that the specification allegedly does not adequately describe the fusion genes such as structure and hybridization conditions.

Applicants submit that the presently claimed invention is adequately supported and taught by the specification. Applicants have amended the claims to be commensurate in scope with the disclosure in the specification.

Applicants claim a transgenic mollusk whose genome comprises a nucleic acid construct that has a promoter linked to a foreign pigment gene, which causes the mollusk to express the pigment gene in the form of fluorescence in the mantel of the mollusk. The foreign gene, which encodes GFP (Green Fluorescent Protein), is fused with another protein gene. The foreign gene may also be introduced into the mollusk by a vector.

The elements of the present invention are adequately described in the specification at page 3 and page 5, line 13 to page 6, line 6. Please also see the Examples in the specification for producing the mollusk of the present invention. Clearly the invention is adequately described and enabled. However, Applicants also submit that GFP has not been observed in the gills of the mollusk, but has only been observed in the whole mantle tissue. This demonstrates that GFP is integrated into the mantle tissue and expresses fluorescence. Applicants attempted to discover the exact structure

of GFP that is bound or not bound to other molecules, but PCR results were inconclusive. For the foregoing reasons, Applicants submit that this rejection should be withdrawn.

The Examiner also rejects the claims for reciting "shellfish". Applicants amend the claims to narrow the scope of the claims to "transgenic mollusks." As such, the rejection should be withdrawn.

The Examiner also rejects claims 1-8 for not reciting a phenotype for the transgenic mollusks. Applicants submit that although no specific phenotype is disclosed, the specification is still enabling because one of ordinary skill in the art would be able to determine the phenotype with fluorescence by a fluorescent microscope for GFP and with PCR for other genes. As such, Applicants request that this rejection be withdrawn.

Applicants also amend the claims to recite that the protein is secreted by the mantle tissue of the mollusk and not just any tissue of the mollusk. Applicants also amend the claims to specifically recite GFP as the coloring gene. As such, these rejections should also be withdrawn.

Rejection under 35 USC 112, second paragraph

The Examiner rejects claims 1-8 as indefinite. The indefiniteness rejections are regarding claims 1-5. These claims

have been canceled. As such, the rejection is moot and should be withdrawn.

Rejection under 35 USC 102

The Examiner rejects claims 1-4 and 8 as anticipated by Burns et al. USP 5,969,211 (Burns '211). Applicants traverse the rejection and respectfully request the withdrawal thereof.

Applicants submit that the present invention is directed to a transgenic mollusk whose genome comprises a nucleic acid construct that has a promoter linked to a foreign pigment gene, which causes the mollusk to express the pigment gene in the form of fluorescence in the mantel of the mollusk. The foreign gene, which encodes GFP (Green Fluorescent Protein), is fused with another protein gene. The foreign gene may also be introduced into the mollusk by a vector. The invention is also directed to the method of producing the transgenic mollusk.

The amino acid analysis of the actin gene from P. fucata reveals 376 amino acids, but not 165 amino acids from abalone. Oysters, *Crassostrea gigas*, have 379 amino acids in its actin gene. Oyster and pearl oyster actins are similar but do not have the same amino acid composition. They are also different from abalone actin.

In addition the promoter gene from P. fucata has been isolated. This gene also differs from abalone promoter. There is only a 48% maximum matching in both amino acid sequences.

Burns '211 discloses transgenic clams having DNA that encodes galactosidase. Burns fails to disclose transgenic mollusks having a foreign gene, which encodes GFP. As such, Applicants respectfully request that the rejection be withdrawn.

The Examiner also rejects claims 1-3 and 8 as anticipated by Raynter PCT/US95/14685. Applicants traverse the rejection and respectfully request the withdrawal thereof.

Raynter discloses growth agents and coding genes. The promoter used in Raynter is RSV-LTR or mouse metallotionein-I. Raynter fails to disclose transgenic mollusks having a foreign gene, which encodes GFP. Raynter also fails to disclose pearl oyster's promoters for producing totally artificial color pearls. Raynter only mentions growth agents. As such, Applicants respectfully request that this rejection also be withdrawn.

Rejections under 35 USC 103(a)

The Examiner rejects claims 1-5 and 8 as obvious over Burns '211 in view of Godwin. Applicants traverse the rejection and respectfully request the withdrawal thereof.

Applicants rely on the arguments above regarding the deficiencies in Burns '211. Godwin fails to compensate for these

deficiencies. Godwin fails to disclose transgenic mollusks that are pearl producing that have GFP expressed. As such, the rejection should be withdrawn as all the elements of the present invention are not disclosed or suggested by the combination of references.

The Examiner also rejects claims 1-5 and 8 as obvious over Raynter in view of Godwin and Burns '211. Applicants traverse the rejection and respectfully request the withdrawal thereof.

Applicants rely on the arguments above regarding Raynter and Burns '211. Therefore, since Godwin fails to compensate for the deficiencies in both Raynter and Burns '211, Applicants respectfully request that the rejection be withdrawn as all the elements of the present invention are not disclosed or suggested by the combination of references.

The Examiner also rejects claims 1-8 as obvious over Burns '211 in view of Ogawa. Applicants traverse the rejection and respectfully request the withdrawal thereof.

Again, Applicants submit that Burns '211 fails to disclose transgenic mollusks that are pearl producing that have GFP expressed. Ogawa also fails to disclose these elements of the present invention. Ogawa discloses the gene expression of lacZ injected directly into mouse testis with plasmids encapsulated with liposomes. In the present invention, no liposome encapsulated plasmids are used for injection into oyster gonads. As such, Ogawa does not compensate for the deficiencies in Burns '211 so that one

of ordinary skill in the art could arrive at the present invention from the combination of disclosures. Therefore, the rejection should be withdrawn.

Conclusion

Applicants further submit that recombinant adenovirsuses as useful vehicles for integrating foreign genes is highly developed. However, the possibility of gene expression with adenovirus in mollusks has not yet been disclosed. Thus, the present invention is novel and nonobvious. As such, as Applicants have addressed and overcome all rejections in the Office Action, Applicants respectfully request that the rejections be withdrawn and that the claims be allowed.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Kecia Reynolds (Reg. No. 47,021) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Attached hereto is a marked-up version of the changes made to the application by this Amendment.

Pursuant to 37 C.F.R. § 1.17 and 1.136(a), Applicants respectfully petition a three (3) month extension of time for

filing a response in connection with the present application. The required fee of $465.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By _____
Gerald M. Murphy, Jr., #28,977

GMM/KJR/jeb
0760-0294P

P.O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000

Attachment: Version with Markings to Show Changes Made

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The paragraph bridging pages 6-7 (page 6, line 27, page 7, lines 1-25), was replaced with the following rewritten paragraph:

--Human or mouse interferon α gene (commercially available from BBL and RDS, respectively) was inserted into an adenovirus vector (commercially available from TAKARA SHUZO, Takara Adenovirus Expression Vector Kit) to obtain recombinant vectors. This operation was carried out concretely as follows: Each of the above-mentioned commercially available interferon α genes was inserted into the *Swa* I site of a cosmid vector [pAxcwt] pAxCAwt (44,741 bp), Niwa, M. et al., (1991) Gene 108, 193, this cosmid vector is included in the above-mentioned commercially available Adenovirus Expression Vector Kit). The cosmid vector having the inserted gene and the above-mentioned commercially available adenovirus-derived DNA-TPC (Miyake, S. et al., (1996), Proc. Natl. Acad. Sci. USA 93 1320) digested with the above-mentioned restriction enzyme were co-transfected into 293 cells (human fetal kidney cell, commercially available from DAINIPPON PHARMACEUTICAL CO., LTD). The 293 cells were cultured in 10% FCS-containing DMEM medium under 5% CO_2 at 37°C until 100% confluency is achieved, and 10 μg of the above-mentioned cosmid vector DNA and 5 μg of the restriction enzyme-treated DNA-TPC were mixed on a petri dish with

a diameter of 6 cm. The transfection was carried out by the calcium phosphate method. The cells after the co-transfection were cultured at 37°C under 5% CO_2 for 24 hours, and the fragment of grown recombinant adenovirus was recovered. The collected fragment was injected into ovaries of *Pinctada fucata Martensii* in an amount of 100 to 200 mg DNA/ovary. Sperms (twice amount of eggs) were mixed with the eggs in a test tube to carry out fertilization. The resulting eggs were cultured in sea water at 25°C for 24 days to obtain young shells. In 31 young shells among 200 young shells, fluorescence (FITC) of a DNA probe for detecting interferon gene was observed. The DNAs of these young shells were purified and existence of the sequence was confirmed with the same DNA probe. These shells were continued to be cultivated.

IN THE CLAIMS:

Claims 1-5 were cancelled.

6. (Twice Amended) A method for producing the [transgeneic] transgenic mollusk according to claim [1] 10, comprising microinjecting into gonad of male and/or female of mollusk a recombinant vector into which a desired foreign gene to be introduced [or a nucleic acid containing said foreign gene is inserted]; crossing said male and female to produce individuals of first generation; and selecting therefrom (an) individual(s) which express(es) said desired gene.

8. (Twice Amended) A method for producing the transgenic mollusk according to claim [1] 11, comprising introducing into unfertilized eggs, fertilized eggs or embryos of a mollusk to be transformed a recombinant vector into which a nucleic acid including a promoter having a promoter activity in said mollusk and said desired gene located at a downstream region of said promoter and functionally linked to said promoter is inserted; developing said unfertilized eggs, fertilized eggs or embryos to individuals; and selecting therefrom (an) individual(s) which express(es) said desired gene.

Claims 9-17 were added.